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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/823,263
Filing Date: April 13, 2004
Appellant(s): LATTA, PAUL P.

Daniel E.Altman
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 07/25/06 appealing from the Office action mailed 11/03/05.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

10/660,924

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US Patent 6,703,017

US Patent 5,425764

US Patent 5,629,194

US Patent 5,529,914

Posselt et al ., Ann Surg. 1991, Vol.214 pages 363-373

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Issue I

Claims 1-4 and 6 –11, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,703,017 or by US Patent 5,425764 or US Patent 5,629,194 each in view Posselt et al (Ann Surg. 1991, Vol.214 pages 363-373).

US Patent '017 teaches a method of treating diabetes in a mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract and columns 6, 8, 9 –14 and Example 12 in particular) . US Patent '017 teaches that insulin producing cells are pancreatic islet cells from primary cell source (see columns 8 and 11 in particular). US Patent '017 teaches that pancreatic islet cells are from the same species as the mammal and are implanted interperitoneally into the tissue of a mammal beneath the kidney capsule (see overlapping columns 13-14 and Example 2 in particular). US Patent '017 teaches that encapsulation of said insulin-producing cells in biologically compatible membrane for success of implantation is well known in the art (see column 12 and Example 12 in particular).

US Patent '764 teaches a method of treating diabetes in a mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract and overlapping columns 5-6 in particular). US Patent '764 teaches that insulin producing cells are pancreatic islet cells (see column 1 and 4 in particular). US Patent '764 teaches that cells are implanted interperitoneally (see column 5 in particular).

US Patent '194 teaches a method of treating diabetes in mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract overlapping columns 7-8 , 12 and Example II in particular). US Patent '764 teaches that insulin producing cells are pancreatic islet cells (see column 8 in particular). US Patent '764 teaches that cells are implanted intaportal (see column 7 in particular). US Patent '194 teaches administration of one or more anti-inflammatory agent at the dosage sufficient to achieve the desired therapeutic effect. US Patent '194 teaches that said agent can be administered prior to, at the same time or subsequent to administration of insulin-producing cells (see overlapping columns 14-15 in particular).

US Patent '017 or US Patent ' 764 or US Patent '194 does not explicitly teaches a method of treating diabetes in a mammal comprising administration two doses of insulin-secreting cells one tolerizing dose and one therapeutic dose wherein tolerizing doze is one order less than therapeutic dose.

Posselet et al., teach that the important goal in the treatment of insulin-dependent diabetes by pancreatic islet transplantation is the development of strategies that allow permanent survival of pancreatic islet without continuous host immunosuppression. Posselet et al., further teach a strategy comprising two step process : first administering a small dose of cells that induces an unresponsive state, i.e. tolerizing dose and then administering fully therapeutic dose, at another site (see entire document, Abstract in particular). Posselet et al., teach that said strategy permits the survival of pancreatic islet transplant.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Posselt at al. to those of US Patent '017 or US Patent ' 764 or US Patent '194 to obtain a claimed method of treating diabetes in a mammal comprising administration two doses of insulin-secreting cells one tolerizing dose and one therapeutic dose wherein tolerizing doze is one order less than therapeutic dose

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because a strategy comprising two step process : first administering a small dose of cells that induces an unresponsive state, i.e. tolerizing dose and then administering fully therapeutic dose, at another site permits the survival of pancreatic islet transplant as taught by Posselet et al. Said strategy can used in the method of treating diabetes in a mammal, comprising implanting pancreatic islet, taught by US Patent '017 or US Patent ' 764 or US Patent '194. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 8-11, 13 and 14 are included because it would be conventional and within the skill of the art to : (i) determine the proper pore size for the permselective membrane or (ii) to determine the optimum dosage and means of administration of insulin-secreting cells in an absent of a showing of unobvious property. Moreover, Applicant acknowledge that one of ordinary skill in the art can readily determine the proper pore size for the permselective membrane (see page 8, line 13-20 of the instant Specification in particular). Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges or means of administration involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Issue II

Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,703,017 or by US Patent 5,425764 or US Patent 5,629,194 each in view Posselt et al (Ann Surg. 1991, Vol.214 pages 363-373) as applied to claims 1-4 and 6-11, 13 and 14 above, and further in view of US Patent 5,529,914

The teaching of US Patent " 017, US Patent ' 764 , US Patent' 194 and Posselt et al., have been discussed, supra.

The combined references do not explicitly teachers a method of treating diabetes in a mammal comprising implanting insulin-secreting cells, wherein insulin-secreting cells are encapsulated in a biologically compatible membrane wherein said membrane comprises polyethylene glycol (PEG).

US Patent '914 teaches a new type of biocompatible membrane as a covering to encapsulate biological materials, comprising PEG that is acceptable for implants in mammalian. (see entire document, Abstract in particular). US Patent '914 teaches that various types of cells can be encapsulated in said biocompatible membrane and that said encapsulation will prevent rejection of encapsulated cells during transplantation (see column 10 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '914 to those of US Patent " 017, US Patent ' 764 , US Patent' 194 and Posselt et al., to obtain a claimed method of treating diabetes in a mammal comprising implanting insulin-secreting cells, wherein insulin-secreting cells are encapsulated in a biologically compatible membrane wherein said membrane comprises polyethylene glycol (PEG).

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because encapsulation of cells in biologically compatible membrane comprising PEG will prevent rejection of encapsulated cells during transplantation as taught by US Patent '914. Said type of biocompatible membrane can be used to substitute the different type of biocompatible membrane for successful implantation of insulin-producing cells in the method of treating diabetes taught by combined references of US Patent " 017, US Patent ' 764 , US Patent' 194 and Posselt et al. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(10) Response to Argument

Issue I

Claims 1-4 and 6 –11, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,703,017 or by US Patent 5,425764 or US Patent 5,629,194 each in view Posselt et al (Diabetes, 1992, v.41, pages 771-775).

An page 4 of the Brief, Appellant argues that none of the primary references cited by the Examiner provide any teaching of a tolerizing dose followed by the therapeutic dose. All of these patents teach only the administration of a single fully- therapeutic dose.

At page 6 of the Brief, Appellant argues that although Posselt et al., does disclose a two-step process of administering insulin-producing cells, the initial tolezing dose in not one or two orders of magnitude less than therapeutic dose, as recited in pending claim 3. Appellant further asserts that in Posselt et al., the only implantation site that showed survival of the implanted cells was the thymus. There is no indication of any kind in Posselt et al., that any site other than thymus can be used to induce immunological torerance. Thus, according to Appellant, Posselt et al., teaches away from using the initial dose of insulin-producing cells anywhere but thymus.

At page 8 of the Brief, Appellant asserts that the instant claims by recitation that impanting is " subcapsular, subcutaneous, intaperitoneal or intraportal" exclude implanting into the thymus.

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

It is also noted that Appellant's own statement that Posselt et al., does disclose a two-step process of administering insulin-producing cells wherein the first dose is a tolerizing dose confirmed the Examiner position.

The issue raised by the Examiner was that all primary references do not teach **a two-step process,** i.e. tolerizing and then therapeutic.

As has been stated supra, US Patent '017 teaches a method of treating diabetes in a mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract and columns 6, 8, 9 –14 and Example 12 in particular) . US Patent '017 teaches that insulin producing cells are pancreatic islet cells from primary cell source (see columns 8 and 11 in particular). US Patent '017 teaches that pancreatic islet cells are from the same species as the mammal and are implanted interperitoneally into the tissue of a mammal beneath the kidney capsule (see overlapping columns 13-14 and Example 2 in particular). US Patent '017 teaches that encapsulation of said insulin-producing cells in biologically compatible membrane for success of implantation is well known in the art (see column 12 and Example 12 in particular).

US Patent '764 teaches a method of treating diabetes in a mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract and overlapping columns 5-6 in particular). US Patent '764 teaches that insulin producing cells are pancreatic islet cells (see column 1 and 4 in particular). US Patent '764 teaches that cells are implanted interperitoneally (see column 5 in particular).

US Patent '194 teaches a method of treating diabetes in mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract overlapping columns 7-8 , 12 and Example II in particular). US Patent '764 teaches that insulin producing cells are pancreatic islet cells (see column 8 in particular). US Patent '764 teaches that cells are implanted intaportal (see column 7 in particular). US Patent '194 teaches administration of one or more anti-inflammatory agent at the dosage sufficient to achieve the desired therapeutic effect. US Patent '194 teaches that said agent can be administered prior to, at the same time or subsequent to administration of insulin-producing cells (see overlapping columns 14-15 in particular).

US Patent '017 or US Patent ' 764 or US Patent '194 does not explicitly teaches a method of treating diabetes in a mammal comprising administration two doses of insulin-secreting cells one tolerizing dose and one therapeutic dose wherein tolerizing doze is one order less than therapeutic dose.

It is the examiner position, that has been confirmed by Appellant's own statements, that Posselet et al., teach a two-step stratergy: first administering a small dose of cells that induces an unresponsive state, i.e. tolerizing dose and then administering fully therapeutic dose. The administering site of said initial dose should be different from the site of administering of second therapeutic dose. Posselet et al., teach that said strategy permits the survival of the second therapeutic dose of pancreatic islet from either rejection or autoimmunity (see page 365 in particular). The fact that Posselet et al., implanted the first, i.e. tolerizing dose into thymus does

not neglect the general teaching of said reference, i.e. **the advantages of using the two-step process it treating diabetes in a mammal**. Posselet et al., teach that the important goal in the treatment of insulin-dependent diabetes by pancreatic islet transplantation is the development of strategies that allow permanent survival of pancreatic islet without continuous host immunosuppression.

Moreover, it is noted that the language of pending claim 1 does not exclude implanting of tolerizing dose of insulin-secreting cells into the thymus. The recitation of specific means of implanting i.e. subcapsular, subcutaneous, intaperitoneal or intraportal does not exclude implantation into the thymus, since the instant claim 1 recites an open term "comprising".

In addition, contrary to Appellant's assertion, there is no indication or suggestion in Posselt et al., that only intrathymic transplantation should be performed. Posselt et., teach that the finding that recipient bearing established intrathymic graft **fail to destroy subsequent extrathymic islets** either by rejection or autoimmunity argues that additional mechanism that alter systemic immune response are also involved. In other words, one skill in the art would immediately recognized that Posselt et., teach an **advantages of using the two-step process it treating diabetes in a mammal**, i.e. administering a small tolerizing dose of insulin-secreting cells in one place and followed by administering a full therapeutic dose of said insulin-secreting cells into the different place. Said strategy will allow permanent survival of implanting therapeutic dose of pancreatic islet without continuous host immunosuppression. Though Posselt et., do not explicitly teach that tolerizing dose should be one or two orders of magnitude less than therapeutic dose, one skill in the art would be able to determine the optimal ratio of tolerizing: therapeutic dose. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Posselt at al. to those of US Patent '017 or US Patent ' 764 or US Patent '194 to obtain a claimed method of treating diabetes in a mammal comprising administration two doses of insulin-secreting cells one tolerizing dose and one therapeutic dose wherein tolerizing doze is one order less than therapeutic dose

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because a strategy comprising two step process : first administering a small dose of cells that induces an unresponsive state, i.e. tolerizing dose and then administering fully therapeutic dose, at another site permits the survival of pancreatic islet transplant as taught by Posselet et al. Said strategy can used in the method of treating diabetes in a mammal, comprising implanting pancreatic islet, taught by US Patent '017 or US Patent ' 764 or US Patent '194. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 8-11, 13 and 14 are included because it would be conventional and within the skill of the art to : (i) determine the proper pore size for the permselective membrane or (ii) to determine the optimum dosage and means of administration of insulin-secreting cells in an absent of a showing of unobvious property. Moreover, Applicant acknowledge that one of

ordinary skill in the art can readily determine the proper pore size for the permselective membrane (see page 8, line 13-20 of the instant Specification in particular). Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges or means of administration involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Issue II

Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,703,017 or by US Patent 5,425764 or US Patent 5,629,194 each in view Posselt et al (Ann Surg. 1991, Vol.214 pages 363-373) as applied to claims 1-4 and 6-11, 13 and 14 above, and further in view of US Patent 5,529,914.

At page 9 of the Brief, Appellant asserts that since claim 1 has been improperly rejected under U.S.C. 103(a) , dependent claim 5 is in compliance with U.S.C. 103(a).

As have been discussed, supra, it is the Examiner position that base claim 1 has been properly rejected under U.S.C. 103(a) being unpatentable over US Patent 6,703,017, US Patent 5,425764 US Patent 5,629,194 each in view of Posselt et al.

The combined references do not explicitly teachers a method of treating diabetes in a mammal comprising implanting insulin-secreting cells, wherein insulin-secreting cells are encapsulated in a biologically compatible membrane wherein said membrane comprises polyethylene glycol (PEG).

US Patent '914 teaches a new type of biocompatible membrane as a covering to encapsulate biological materials, comprising PEG that is acceptable for implants in mammalian. (see entire document, Abstract in particular). US Patent '914 teaches that various types of cells can be encapsulated in said biocompatible membrane and that said encapsulation will prevent rejection of encapsulated cells during transplantation (see column 10 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '914 to those of US Patent " 017, US Patent ' 764 , US Patent' 194 and Posselt et al., to obtain a claimed method of treating diabetes in a mammal comprising implanting insulin-secreting cells, wherein insulin-secreting cells are encapsulated in a biologically compatible membrane wherein said membrane comprises polyethylene glycol (PEG).

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because encapsulation of cells in biologically compatible membrane comprising PEG will prevent rejection of encapsulated cells during transplantation as taught by US Patent '914. Said type of biocompatible membrane can be used to substitute the different type of biocompatible membrane for successful implantation of insulin-producing cells in the method of treating diabetes taught by combined references of US Patent " 017, US Patent ' 764 , US Patent' 194 and Posselt et al. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained

Respectfully submitted,

Michail Belyavskyi,
Art Unit 1644
November 7, 2006

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